

REMARKS

Claims 26-29 and 31-46 are pending following entry of this Amendment. Claims 28, 33 and 38 are the only pending independent claims. Applicants appreciate the Examiner's indication in Section 1 of the Detailed Action that claims 29, 33 and 34 have been examined, in effect withdrawing the restriction or election requirement concerning these claims. Although claims 26 and 27 still have been withdrawn by the Examiner, reconsideration, examination and allowance of claims 26 and 27 are sought for the reasons noted below.

Explanation of and Support for Amended and New Claims in the Specification

Claim 28 has been amended, without prejudice, to indicate that the protein consists of, rather than comprises, the recited elements. As such, claim 28 encompasses a protein that has any combination of each of at least one of an entire conserved region (C1-C5) and at least one of an entire variable region (V1-V4), but has at least one V region deletion usually present in wild-type NhhA protein. Amended claim 28 is supported as set forth in the Amendment filed June 30, 2003.

Claim 29 has been amended to recite the particular embodiments SEQ ID NOS: 26 and 38 of claim 28 that are described in the Examples.

Claims 33 and claim 34, which depended and still depends from claim 33, were considered to obtain allowable subject matter, but were objected to by the Examiner as ultimately depending from previously-rejected claim 28. Since claims 33 and 34 always claimed specific sequences, claim 33 has been amended into a stand-alone independent claim. Incorporating language from previously presented claim 28 would not have added anything significant to claim 33. Accordingly, claims 33 and 34 should now be in full condition for allowance.

Claims 35 and 36 have been amended to recite that the 20% or 10% variation, respectively, would be restricted to residues that are non-conserved in SEQ ID NO:11 (*i.e.* the amino acids marked "X"). The amendments are supported by the respective sequence listings.

New claim 37 claims an isolated fusion protein comprising the isolated protein of claim 28 and at least one fusion partner protein. This claim is supported by the description at least at

page 20, line 25, to page 21, line 31, and is in part included due to the use of the “consisting of” language in claim 28.

New generic claim 38 corresponds to claim 28, with additional revisions. In all of the Examples, if a V1 region is present in a mature protein then only residues 52-54 are present. If the protein is an immature unprocessed protein it also has residue 51 of V1 (*i.e.* it has residues 51-54 of V1). Also, if C3 is present in either a mature or immature protein then only residues 144-198 of this region are present. The 144-198 residues of C3 are produced as a result of the recombinant deletion process (see Examples 4 and 5 and SEQ ID NOS: 23, 35, 24 and 36).

New claim 38 has been drafted to encompass a protein that has any combination of at least one of the entire C2, C4 or C5 regions and/or the 144-198 fragment of C3 and at least one of the entire V2-V4 regions and/or amino acids 52-58 ~~4~~ of V1 and/or amino acid 51 of V1.

Thus, new claim 38 would generically encompass the mature, processed forms SEQ ID NOS: 35, 36 and 38 and their corresponding immature forms SEQ ID NOS: 23, 24 and 26. Claim 38 excludes any protein composed entirely of C regions, namely SEQ ID NOS: 25, 27, 37 and 39 or having no V1 region amino acids deleted, namely SEQ ID NOS: 33 and 34.

Claim 38 also now specifies that V1 is either absent, or that only amino acids 52-54 of V1 and/or residue 51 are present. This is also supported by the statement at page 11 line 31 to page 12 line 4. The 52-54 fragment of V1 is produced as a result of the recombinant deletion process (see Examples 4 and 5 and SEQ ID NOS: 23, 35, 24 and 36). Residue 51 is present together with C1 (1-50) in immature forms of the protein.

Compared to claim 28, in claim 38 the language “wherein the isolated protein has at least one fewer variable regions than a wild-type NhhA polypeptide” has been removed because claim 38 does not necessarily exclude an entire V region.

In light of claim 38, claim 39, which depends from claim 38, has been amended to delete SEQ ID NOS: 25, 26, 33, 34 and 37, which do not fall within the scope of claim 38.

Claims 40 and 41 correspond to claims 35 and 36, and recite that the respective 20% or 10% variation would be restricted to residues that are non-conserved in SEQ ID NO:11 (*i.e.* the amino acids marked “X”).

New claim 42 is similar to claim 27 and recites the specific C region sequences of SEQ ID NOS:1-10 that are encompassed by the C regions (and C3 fragment) of claim 38.

New claim 43 recites the specific V region sequences of SEQ ID NOS:1-10 that are encompassed by the V regions (and 52-54 V1 portion) of claim 38. Residue 51 has not been claimed individually in each of SEQ ID NOS: 1-10, as it can only be an Ala or Thr residue.

New claim 44 is simply a claim to the isolated protein of claim 38 that has an additional fusion partner protein, and corresponds to new claim 37, discussed above, that depends from claim 28.

New claims 45 and 46 are claims to pharmaceutical compositions comprising the isolated protein of claim 38. They correspond to previously presented and currently pending claims 31 and 32. They are supported, for example, at page 32, line 6, through page 37, line 18.

Since all of the amendments and new claims 37-46 are fully supported by the application as filed, no new matter has been added and entry of the amendments is respectfully solicited.

Restriction and Election of Species

Although the Examiner effectively withdrew the restriction and election requirements relating to claims 29, 33 and 34, the requirements were retained regarding claims 26 and 27, both of which depend from generic claim 28, without comment in the Office Action. Apparently, the Examiner maintains her conclusion that these claims are directed to non-elected species. However, as pointed out in the last Amendment filed June 30, 2003, in paragraph 1 at page 2 of the Office Action of January 17, 2003 (Paper No. 18), the Examiner asserted that Applicants "elected without traverse of Group II, claims 10-16, SEQ ID NO:11, residues 109, 120," in their response filed April 22, 2002, and concluded that because of this, claims 26, 27 and 29 were not examined because they are directed to non-elected species, even though a requirement to elect specific residues was withdrawn in a previous Office Action.

Applicants respectfully point out to the Examiner that her quoted assertion is not fully accurate. In the Amendment filed April 22, 2002, it was only Group II, claims 10-16, which were elected without traverse, but Applicants provisionally elected, with traverse to prosecute SEQ ID NO:11, residues 109-120. As noted in the Final Rejection of January 17, 2003, the requirement to elect specific residues (*i.e.*, residues 109-120) had already been withdrawn in a previous Office Action. Accordingly, the basis for the Examiner's determination that claims 26, 27 and 29 are directed to a non-elected species, appears not to be well-founded. Applicants again respectfully remind the Examiner that SEQ ID NO: 11 is a consensus sequence that, by its definition (*e.g.*, see the sequence listing) incorporates each of SEQ ID NOS: 1-10. Claim 26,

directed to a protein of claim 28 comprising at least 12 contiguous amino acids of a sequence from SEQ ID NOs:1-10 is clearly contemplated as being within a consensus SEQ ID NO:11. See Table 1 at page 55 and the sequence listing, where at least 12 contiguous amino acids are fully set forth. Similarly, the residue alignment of SEQ ID NO:11 in Table 1 supports the residue alignment claimed in claim 27. Moreover, claim 27 corresponds to original elected claim 11.

Response to Rejections

Each rejection will now be addressed in turn.

Written Description

The Examiner has essentially reiterated her previous comments regarding the broad scope of previous claim 28, using the open-ended term “comprising”, rather than the term “consisting” in the present amendment, and claims 35 and 36 directed to variants of the claim 28 protein.

In response, claim 28 as now amended recites that each C and V region consists of the indicated amino acid residues. Thus, the written description supports the full scope of claim 28 as amended.

The rejection of claims 35 and 36 was based on the Examiner’s assertion that there is no teaching as to which amino acids may be varied and which may not. Claims 35 and 36 as now amended are more explicit about which amino acids are conserved and which are variable.

New independent claim 38, also using the “consisting of” language, is even more specific with respect to the C and V regions of the claimed protein than claim 28. That is, the exact boundaries of the C1-5 and V2-4 regions are defined, fragments (other than residues 51 and/or 52-54 of V1 and 144-198 of C3) are excluded and variants are restricted to those where variability occurs in only those amino acids indicated as being non-conserved in SEQ ID NO:11. Likewise, new claims 40 and 41, corresponding to claims 35 and 36, are also fully supported by the written description.

Applicants believe that the claims as now amended comply entirely with the Examiner’s suggestions regarding the written description. Accordingly, Applicant respectfully request reconsideration and withdrawal of the written description and any other rejections under 35 U.S.C. § 112.

Novelty 35 U.S. C. § 102(e) - US patent 6,197,312 (Peak)

For the purpose of this response, Applicants will assume only for the sake of argument, without waiver or acquiescence, that Peak is appropriate prior art under 35 U.S. C. § 102(e), but Applicants reserve the right to file appropriate documents swearing behind or otherwise addressing the status of Peak as prior art to this application.

As the rejection is understood, it appears that the Examiner is not asserting that Peak discloses the precise C and V regions as set forth in former claim 28 (which it does not). More specifically with regard to amended claim 28, Peak does not “consist of” the C and V regions as now claimed in claim 28. Moreover, with respect to new claim 38, the idea of deleting V1 (or residues 51 and/or 54-108 thereof), is not taught or even suggested by Peak. Applicants respectfully submit that it is not appropriate for the Examiner to rely on general language in the disclosure of Peak regarding “fragments, variants and derivatives” as anticipating the formerly pending claims, let alone the claims as now amended. There is simply no disclosure in Peak to the effect that V1 (or residues 51 and/or 54-108 thereof) should be targeted for deletion.

The isolated protein of amended claim 28 and new claim 38 consists of the recited C and V regions, and Peak neither teaches nor even suggests such a protein.

Amended claim 29 defines subject matter that is novel in view of Peak, in that Peak does not teach or suggest the particular sequences of SEQ ID NO:26 or SEQ ID NO:38. The concluding remarks of the Examiner (bottom of page 7 of the Office Action) seem to suggest that SEQ ID NO:34 (now deleted) was the specific problem with claim 29.

New claim 39, deleting, among others, SEQ ID NO:34, which is simply a wild-type NhhA protein minus the N-terminal C1 region leader peptide, is novel in that Peak does not teach or suggest the particular sequences of SEQ ID NOS:23, 24, 26, 35, 36 or 38.

Applicants believe that amended claims 35 and 36, and new claims 40 and 41, which very specifically recite exactly which residues can be varied, are novel in light of the general disclosure of “fragments” and “variants” recited in Peak.

Applicants respectfully request reconsideration and withdrawal of the anticipation rejections based on Peak.

Novelty 35 U.S. C. § 102(a) - International Publication WO 99/36544 ((Masignani))

The Examiner has raised Masignani for the first time in the outstanding Office Action, and has concluded that Masignani anticipated prior claims 28, 30-32, 35 and 36. Applicants do not understand why Masignani was considered to anticipate claim 28, given that SEQ ID NO:4

(or any of the other sequences) in Masignani does not have a V region deletion or part deletion as set forth in previous claim 28, amended claim 28 or new claim 38.

Whatever the case, the comments above regarding Peak apply equally here when bearing in mind the claims as now amended. Thus, the isolated protein of amended claim 28 consists of the recited C and V regions, and Masignani neither teaches nor suggests any such protein.

U.S. Patent 6,709,660 B1, which issued March 23, 2004, and which is submitted contemporaneously herewith under separate cover with a Second Supplemental Information Disclosure Statement, claims priority from Masignani. It is not believed that this patent, even assuming only for the sake of argument that it is prior art with respect to the present application, discloses or suggests anything that would render the presently claimed invention unpatentable.

Applicants respectfully request the Examiner to reconsider and withdraw all of the prior art rejections based on all of the cited prior art.

Conclusion

Applicants believe that all of the pending claims are in condition for allowance. Reconsideration and withdrawal of all of the rejections and objections, and allowance of these claims are respectfully requested at the earliest possible time.

Respectfully submitted,

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Enclosures:

Petition for Three-Month Extension of Time and Extension Fee
Second Supplemental Information Disclosure Statement with cited reference

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